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TOWNSEND and TOWNSEND and CREW LLP

By: /Aaron Hokamura/

**PATENT**  
Attorney Docket No.: 15280W-  
002100US  
Client Reference No.: E-286-1998/1-US-  
06

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

BRENNEMAN et al.

Application No.: 10/049,587

Filed: February 12, 2002

For: ORALLY ACTIVE PEPTIDES  
THAT PREVENT CELL DAMAGE AND  
DEATH

Confirmation No.: 9701

Examiner: Standley, Steven H.

Art Unit: 1649

**INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. Copies of references AA - AG are not provided, in compliance with the provisions of 37 CFR §1.98(a)(2). Copies of references AH - CC are provided herewith.

It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR §1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

This IDS is being filed before the mailing date of the final Office Action or Notice of Allowance.

Please charge the IDS fee of \$180 to Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,

/Beth L. Kelly/

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TOWNSEND and TOWNSEND and CREW LLP  
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Substitute for form 1449A/PTO <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>				<b>Complete if Known</b>	
Sheet	1	of	6	Application Number	10/049,587
				Filing Date	February 12, 2002
				First Named Inventor	Brenneman, Douglas
				Art Unit	1649
				Examiner Name	Standley, Steven H.
				Attorney Docket Number	15280W-002100US

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number Kind Code <sup>2</sup> (if known)				
	AA	4,587,046		05-06-1986	Goodman et al.	
	AB	5,767,240		06-16-1998	Brenneman et al.	
	AC	6,174,862 B1		01-16-2001	Brenneman	
	AD	6,613,740 B1		09-02-2003	Gozes et al.	
	AE	6,933,277 B2		08-23-2005	Brenneman et al.	
	AF	2004/0048801 A1		03-11-2004	Spong et al.	
	AG	2004/0053313 A1		03-18-2004	Gozes et al.	

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	AH	WO	92/18140	A1	10-29-1992	The United States of America, represented by The Secretary, Department of Health and Human Services		<input type="checkbox"/>
	AI	WO	96/11948	A1	04-25-1996	The Government of the United States of America, as represented by the Secretary of the Department of Health and Human Services		<input type="checkbox"/>
	AJ	WO	98/35042	A1	08-13-1998	The Government of the United States of America, represented by the Secretary of the Department of Health and Human Services		<input type="checkbox"/>
	AK	WO	00/27875	A2	05-18-2000	The Government of the United States of America as represented by the Secretary of the Department of Health and Human Services; and Ramot University Authority for Applied Research and Industrial Development		<input type="checkbox"/>
	AL	WO	00/53217	A2	09-14-2000	The Government of the United States of America, as represented by the Secretary of the Department of Health and Human Services; and Ramot of Tel Aviv University		<input type="checkbox"/>
	AM	WO	01/12654	A2	02-22-2001	Ramot University, Authority for Applied Research & Industrial Development Ltd.; and The Government of the United States of America, represented by the Department of Health and Human Services		<input type="checkbox"/>

Examiner Signature		Date Considered	
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<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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Sheet	2	of	6	Attorney Docket Number	15280W-002100US

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		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	AN	EP	1 206 489	B1	05-06-2004	Ramot University, Authority for Applied Research & Industrial Development Ltd.; and The Government of the United States of America, represented by the Department of Health and Human Services		<input type="checkbox"/>

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Substitute for form 1449B/PTO				<b>Complete if Known</b>	
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Sheet	3	of	7	<i>Attorney Docket Number</i>	15280W-002100US

<b>NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
		T <sup>2</sup>			
	AO	Bassan, M. et al. "VIP-Induced Mechanism of Neuroprotection: The Complete Sequence of a Femtomolar-Acting Activity-Dependent Neuroprotective Protein." <i>Regulatory Peptides</i> , Vol. 71, No. 2, (August 15, 1997).			<input type="checkbox"/>
	AP	Bassan, M. et al. "Complete Sequence of a Novel Protein Containing a Femtomolar-Activity-Dependent Neuroprotective Peptide." <i>Journal of Neurochemistry</i> , Vol 72, pp. 1283-1293 (1999)			<input type="checkbox"/>
	AQ	Beni-Adani, L. et al. "Activity-Dependent Neurotrophic Protein is Neuroprotective in a Mouse Model of Closed Head Injury." Society for Neuroscience, 28 <sup>th</sup> Annual Meeting, Los Angeles, CA, November 7-12, 1998. <i>Abstracts</i> , Vol. 23, Part 1, p. 1043 (1998).			<input type="checkbox"/>
	AR	Brenneman, D.C. and Gozes, I. "A Femtomolar-Acting Neuroprotective Peptide." <i>Journal of Clinical Investigation</i> , Vol. 97, pp. 2299-2307 (1996)			<input type="checkbox"/>
	AS	Brenneman et al. "Neuronal Cell Killing by the Envelope Protein of HIV and Its Prevention by Vasoactive Intestinal Peptide." <i>Nature</i> 335:636 (1988)			<input type="checkbox"/>
	AT	Brenneman et al. "N-Methyl-D-Aspartate Receptors Influence Neuronal Survival in Developing Spinal Cord Cultures" <i>Dev. Brain Res.</i> 51:63 (1990).			<input type="checkbox"/>
	AU	Brenneman, D.E. et al. "Identification of a Nine Amino Acid Core Peptide from Activity Dependent Neurotrophic Factor I." Society for Neuroscience, 27 <sup>th</sup> Annual Meeting, New Orleans, LA, October 25-30, 1997. <i>Abstracts</i> , Vol. 23, Part 2, p. 2250 (1997).			<input type="checkbox"/>
	AV	Brenneman, D.E. et al. "Activity-Dependent Neurotrophic Factor: Structure-Activity Relationships of Femtomolar-Acting Peptides." <i>Journal of Pharmacology and Experimental Therapeutics</i> , Vol. 285, pp. 619-627 (1998)			<input type="checkbox"/>
	AW	Davidson, A. et al. "Protection Against Developmental Retardation and Learning Impairments in Apolipoprotein E-Deficient Mice by Activity-Dependent Femtomolar-Acting Peptides." Society for Neuroscience, 27 <sup>th</sup> Annual Meeting, New Orleans, LA, October 25-30, 1997. <i>Abstracts</i> , Vol. 23, Part 2, p. 2250 (1997).			<input type="checkbox"/>
	AX	Dibbern, D.A., Jr. et al. "Inhibition of Murine Embryonic Growth by Human Immunodeficiency Virus Envelope Protein and Its Prevention by Vasoactive Intestinal Peptide and Activity-Dependent Neurotrophic Factor." <i>Journal of Clinical Investigation</i> , Vol. 99, pp. 28377-2841 (1997)			<input type="checkbox"/>
	AY	GenBank Accession No. AB018327 from the DNA Data Bank of Japan (DDBJ) (released November 17, 1998)			<input type="checkbox"/>
	AZ	Giladi, E. "Protection Against Developmental and Learning Impairments in Apolipoprotein E-Deficient Mice by Activity-Dependent Femtomolar-Acting Peptides." <i>Neuroscience Letters</i> , Supplement 48 S1-S60, P. S19 (1997).			<input type="checkbox"/>

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Sheet	4	of	7	<i>Attorney Docket Number</i>	15280W-002100US

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Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		
	BA	Glazner, G.W. et al. "A 9 Amino Acid Peptide Fragment of Activity-Dependent Neurotrophic Factor (ADNF) Protects Neurons from Oxidative Stress-Induced Death." Society for Neuroscience, 27 <sup>th</sup> Annual Meeting, New Orleans, LA, October 25-30, 1997. <i>Abstracts</i> , Vol. 23, Part 2, p. 2249 (1997). <input type="checkbox"/>		
	BB	Glazner, G.W. et al. "Activity Dependent Neurotrophic Factor: A Potent Regulator of Embryonic Growth." <i>Anat. Embryol.</i> 200:65-71 (1999). <input type="checkbox"/>		
	BC	Gozes, I. and Brenneman, D.E. "Activity-Dependent Neurotrophic Factor (ADNF)." <i>Journal of Molecular Neuroscience</i> , Vol. 7, pp. 235-244 (1996). <input type="checkbox"/>		
	BD	Gozes, I. et al. "Stearyl-Norleucine-Vasoactive intestinal Peptide (VIP): A novel VIP Analog for Noninvasive Impotence Treatment." <i>Endocrinology</i> , Vol. 134, pp. 2125 (1994). <input type="checkbox"/>		
	BE	Gozes, I. et al. "Superactive Lipophilic Peptides Discriminate Multiple Vasoactive intestinal Peptide Receptors." <i>Journal of Pharmacology and Experimental Therapeutics</i> , Vol. 273, pp. 161-167 (1995). <input type="checkbox"/>		
	BF	Gozes, I. et al. "Neuroprotective Strategy for Alzheimer Disease: Intranasal Administration of a Fatty Neuropeptide." <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 93, pp. 427-432 (1996). <input type="checkbox"/>		
	BG	Gozes I. et al. "Antiserum to Activity-Dependent Neurotrophic Factor Produces Neuronal Cell Death in CNS Cultures: Immunological and Biological Specificity." <i>Developmental Brain Research</i> , Vol. 99, pp. 167-175 (1997). <input type="checkbox"/>		
	BH	Gozes, I. et al. "A Femtomolar-Acting Activity-Dependent Neuroprotective Protein (ADNP)." <i>Neuroscience Letters</i> , Supplement 48 S1-S60, p. S21 (1997) <input type="checkbox"/>		
	BI	Gozes, I. et al. "Protection Against Developmental Retardation in Apolipoprotein E-Deficient Mice by a Fatty neuropeptide: Implications for Early Treatment of Alzheimer's Disease." <i>Journal of Neurobiology</i> , Vol. 33, pp. 329-342 (1997). <input type="checkbox"/>		
	BJ	Gozes, I. et al. "The cDNA Structure of a Novel Femtomolar-Acting Neuroprotective Protein: Activity-Dependent-Neurotrophic Factor III (ADNFIll)." Society for Neuroscience, 27 <sup>th</sup> Annual Meeting, New Orleans, LA, October 25-30, 1997. <i>Abstracts</i> , Vol. 23, Part 2, p. 2250 (1997). <input type="checkbox"/>		
	BK	Gozes, et al., "A Novel Signaling Molecule for Neuropeptide Action: Activity-dependent Neuroprotective Protein"; Annals of the New York Academy of Sciences, 897:125-135 (1999) <input type="checkbox"/>		
	BL	Gozes, I. et al. "Activity-dependent neurotrophic factor: Intranasal administration of femtomolar-acting peptides improve performance in a water maze" <i>Journal of Pharmacology and Experimental Therapeutics</i> , Vol. 293, pp. 1091-1098 (2000). <input type="checkbox"/>		

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	BM	Gressens, P. et al. "Growth Factor Function of Vasoactive Intestinal Peptide in Whole Cultured Mouse Embryos." <i>Nature</i> 362:155-58 (1993).			<input type="checkbox"/>
	BN	Hannigan, J.H. and Berman, R.F. "Amelioration of Fetal Alcohol-Related Neurodevelopmental Disorders in Rats: Exploring Pharmacological and Environmental Treatments." <i>Neurotoxicol. &amp; Teratol.</i> 22(1):103-111 (2000).			<input type="checkbox"/>
	BO	Hill, J.M. et al. "Learning Impairment in Adult Mice Produced by Early Embryonic Administration of Antisense to Activity-Dependent Neurotrophic Factor (ADNF)." Society for Neuroscience, 27 <sup>th</sup> Annual Meeting, New Orleans, LA, October 25-30, 1997. <i>Abstracts</i> , Vol. 23, Part 2, p. 2250 (1997).			<input type="checkbox"/>
	BP	Lilling, G. et al. "Inhibition of Human Neuroblastoma Growth by a Specific VIP Antagonist." <i>Journal of Molecular Neuroscience</i> , Vol. 5, pp. 231-239 (1995).			<input type="checkbox"/>
	BQ	Mahato et al. "Development of Targeted Delivery Systems for Nucleic Acid Drugs." <i>J. of Drug Targeting</i> 4(6):337-357 (1997) [Abstract]			<input type="checkbox"/>
	BR	McKune, S.K. et al. "Localization of mRNA for Activity-Dependent Neurotrophic Factor III (ADNF III) in mouse Embryo and Adult CNS." Society for Neuroscience, 27 <sup>th</sup> Annual Meeting, New Orleans, LA, October 25-30, 1997. <i>Abstracts</i> , Vol. 23, Part 2, p. 2249 (1997)			<input type="checkbox"/>
	BS	Nagase, et al., "Prediction of the Coding Sequences of Unidentified Human Genes. XI. The Complete Sequences of 100 New cDNA Clones from Brain Which Code for Large Proteins <i>in vitro</i> ," <i>DNA Research</i> 5:277-286 (1998)			<input type="checkbox"/>
	BT	Nelbock, P. et al. "A cDNA for a Protein that Interacts with the Human Immunodeficiency Virus Tat Transactivator." <i>Science</i> , Vol. 248, pp. 1650-1653 (1990).			<input type="checkbox"/>
	BU	Oberdoester, J. et al. "The Effects of Ethanol on Neuronal Cell Death: Implication for the Fetal Alcohol Syndrome." <i>FASEB Journal</i> 12(4):A134 (March 17, 1998).			<input type="checkbox"/>
	BV	Pelsman, A. et al. "In Vitro Degeneration of Down Syndrome neurons is Prevented by Activity-Dependent Neurotrophic Factor-Derived Peptides." Society for Neuroscience, 28 <sup>th</sup> Annual Meeting, Los Angeles, CA, November 7-12, 1998. <i>Abstracts</i> , Vol. 24, p. 1044 (1998)			<input type="checkbox"/>
	BW	Skolnick, J. and Fetrow, J.S. "From Genes to Protein Structure and Function: Novel Applications of Computational Approaches in the Genomic Era." <i>Trends in Biotech.</i> 18(1):34-39 (2000).			<input type="checkbox"/>
	BX	Smith, A.E. "Viral Vectors in Gene Therapy." <i>Ann. Rev. Microbiol.</i> 49:807-838 (1995) [Abstract]			<input type="checkbox"/>

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		T <sup>2</sup>		
	BY	Spinney, L. "New Peptides Prevent Brain Damage." <i>Molecular Medicine Today</i> 5(7):282 (July 1999). <input type="checkbox"/>		
	BZ	Spong <i>et al.</i> "Prevention of Fetal Alcohol Syndrome by Novel Peptides." <i>FASEB Journal</i> 13(5):A881 (March 15, 1991) <input type="checkbox"/>		
	CA	Spong <i>et al.</i> "Prevention of Fetal Demise and Growth Restriction in a Mouse Model of Fetal Alcohol Syndrome" <i>The Journal of Pharmacology and Experimental Therapeutics</i> 297:774-779 (2001) <input type="checkbox"/>		
	CB	Voet <i>et al.</i> <u>Biochemistry</u> , 2nd Ed., p. 67 <input type="checkbox"/>		
	CC	Wilkemeyer <i>et al.</i> "Differential effects of ethanol antagonism and neuroprotection in peptide fragment NAPVSIPQ prevention of ethanol-induced developmental toxicity" <i>PNAS</i> 100:8543-8548 (2003) <input type="checkbox"/>		

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